

Underrecognition and Undertreatment of Atherothrombotic Diseases: REACH Registry Taiwan Baseline Data

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Background/Purpose: Atherothrombosis is a generalized disease affecting different vascular beds, making it the leading cause of death worldwide. To evaluate the long-term risk of atherothrombotic risk factors and determine the predictors for atherothrombotic events, an international, prospective, observational study was initiated, in which Taiwan was involved.

Methods: The REduction of Atherothrombosis for Continued Health (REACH) Registry recruited outpatients with either symptomatic atherothrombotic diseases or multiple risk factors. Baseline data were collected using a universal standard case report form. All subjects were followed to document future outcomes. In this paper, we analyzed the baseline data of the participants from Taiwan.

Results: In the REACH Registry, a total of 67,888 subjects from 44 countries were recruited. Among the 1062 Taiwanese participants, 971 were symptomatic subjects and 91 subjects were with risk factors only (RFO). In comparison with the global participants, the Taiwan patients were younger, with a higher prevalence of males, lower prevalence of hypertension, obesity, hypercholesterolemia, former smokers, and a greater prevalence of non-smokers. The baseline prevalence rates were: hypertension, 46.5%; fasting hyperglycemia, 38.4%; hypercholesterolemia, 45.8%; and hypertriglyceridemia, 42.8%. All these prevalence were higher than the global data, indicating an undertreatment status for the Taiwanese patients. Only 29 (2.7%) peripheral arterial disease (PAD) subjects were recruited in Taiwan, suggesting underrecognition of this disease. The RFO Taiwanese patients had fewer former smokers and more non-smokers than the symptomatic patients, suggesting that smoking may be an important factor contributing to atherothrombotic diseases.

Conclusion: In Taiwan, atherothrombotic outpatients were generally undertreated and PAD was underdiagnosed. [*J Formos Med Assoc* 2007;106(7):548–557]

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Atherosclerosis is a progressive disease affecting the large and medium-sized arteries of the body. At an advanced stage, the lumen of the involved arteries may be severely narrowed, compromising blood supply to the tissues. Or, the atherosclerotic vessel may have thrombus formation on the diseased atherosclerotic inner surface, resulting in sudden severe reduction or even total cessation of blood flow, the process of atherothrombosis. "Atherothrombosis", defined as disruption of an atherosclerotic plaque with superimposed thrombosis^{1,2} was introduced to describe the common underlying vascular occlusive mechanism in different vascular beds. Clinical atherothrombotic diseases may include angina pectoris, and myocardial infarction (MI) secondary to coronary artery disease (CAD), transient ischemic attack (TIA) and cerebral ischemic stroke (CI) resulting from cerebrovascular disease (CVD), and critical limb ischemia due to peripheral arterial disease (PAD).¹ Atherothrombosis is the leading cause of death worldwide, accounting for approximately one-fourth of all-cause mortality in the world in the year 2000,^{3,4} and thus becoming a major public health issue in need of attention.

Many studies have demonstrated the benefits of treating atherothrombotic risk factors for the prevention of cardiovascular or cerebrovascular events. However, randomized controlled trials do not always provide an accurate view of current clinical practice. In contrast, observational studies enable a real-world estimation of actual disease treatments. The Framingham Study,⁵ for example, provides data on risk factors for developing atherothrombosis. However, as most observational studies are restricted to a particular geographic locale, it is difficult to extrapolate data for a global population.

The REduction of Atherothrombosis for Continued Health (REACH) Registry is an international, observational registry initiated to determine whether atherosclerosis risk factor prevalence and treatment would demonstrate comparable patterns in many countries around the world; and, to evaluate the long-term risk of atherothrombosis. The REACH Registry better defined the profile of

subjects at risk of atherothrombosis, the predictors for atherothrombotic events, reinforced the notion that atherothrombosis is a generalized disease, and the importance of the cross risks for atherothrombotic subjects.

The present study compares the baseline data from the Taiwan REACH Registry with the baseline data from the global REACH Registry to characterize Taiwanese patients who either have atherothrombotic diseases or have only multiple atherothrombosis risk factors.

Materials and Methods

The REACH Registry is an international, prospective, observational registry designed to provide 18–24 months of follow-up. Patients were enrolled from 44 countries in the following regions: North America, Latin America, Western Europe, Eastern Europe, Australia, Asia, and the Middle East.

The study recruited outpatients aged 45 years-plus with either documented CAD, CVD and/or PAD, or with at least three atherothrombotic risk factors, over a 7-month period between December 2003 and June 2004. Documented CAD consisted of one or more of the following criteria: stable angina, a history of unstable angina, a history of coronary angioplasty or stenting, a history of coronary artery bypass graft, or previous MI. Documented CVD consisted of a hospital or neurologist report with the diagnosis of TIA or previous CI. Documented PAD consisted of one or both criteria: current intermittent claudication with an ankle brachial index (ABI) < 0.9 or a history of intermittent claudication together with a previous and related intervention (angioplasty, bypass graft, or other vascular intervention, including amputation). Subjects with more than one vascular bed morbidity were eligible for enrolment. Patients without documented atherothrombotic diseases but with at least three of the following atherothrombotic risk factors might also be recruited: type I or II diabetes currently treated with hypoglycemic agents, evidence of diabetic nephropathy (microalbuminuria of $\leq 30 \mu\text{g/mL}$), known

ABI of <0.9 , carotid intima media thickness exceeding twice that of adjacent sites, known asymptomatic carotid stenosis of $\geq 70\%$, systolic blood pressure (SBP) of ≥ 150 mmHg, despite therapy for at least 3 months, hypercholesterolemia currently treated with medication, current smoking of at least 15 cigarettes per day, men aged ≥ 65 years, or women aged ≥ 70 years. The body mass index (BMI) was defined as weight in kilograms divided by the square of height in meters. Subjects with a BMI of 25–29 were considered overweight and subjects with a BMI of ≥ 30 were considered obese. Obese subjects were further classified into class I (BMI, 30 – <35) and class II obesity (BMI, ≥ 35). Another measure of obesity was a waist circumference of ≥ 102 cm (40 inches) in men, or ≥ 88 cm (35 inches) in women. Current smoking was defined as at least 5 cigarettes per day on average within the last month before entry into the REACH Registry; and former smoking was defined as at least 5 cigarettes per day on average for more than 1 month before entry into the REACH Registry; all others were defined as non-smokers.

Subjects already in a clinical trial, hospitalized inpatients, or those who were expected to have difficulty returning for a follow-up visit were excluded from enrolment.

Data were collected from eligible subjects at recruitment using a universal standardized international case report form, including physician profile, demographic information, employment status, medical history, risk factors, physical examination, and current chronic medical treatment at baseline.

Selection of physicians to the REACH Registry was determined at the country level and included: general practitioners or specialists, including cardiologists, neurologists, internists, angiologists, diabetologists, and vascular surgeons. Each physician recruited a maximum of 15 subjects (up to 20 subjects in the United States). Such enrolment allowed extrapolation of the recruitment results to the broadest possible population at risk of atherothrombotic events. In order to ensure that the study population was representative of the overall patient pool, a site selection method was designed and

implemented in each participating country by epidemiologists under supervision of the REACH Registry global and local steering committees and national coordinators. The site selection method accounted for patient profiles, health care environments and medical practices. This was designed to get a good reflection of the burden of atherothrombosis or at-risk populations.

This registry was conducted in accordance with the principles set forth by the 18th World Medical Assembly (Helsinki, 1964) and the protocol was reviewed by the institutional review board as a local request and signed informed consents were obtained from all recruited patients.

Continuous variables are expressed as mean (standard deviation [SD]). Categorical variables are expressed as frequencies and percentages. Comparisons between categorical variables were performed using the Pearson χ^2 test. The *t* test was used to compare continuous variables. Statistical significance level was set at less than 0.05 with a two-tailed probability. Age and gender were adjusted using a logistic regression model. Statistic analysis was performed using SAS software version 8 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 69,055 subjects were enrolled in the REACH Registry from 44 countries in different regions. The distribution of subjects recruited from different regions and the specialty of the recruiting physicians have been published elsewhere.³ Of these recruited subjects, 1109 did not meet the inclusion criteria, and 58 withdrew their consent, leaving 67,888 subjects for data collection and analysis. In Taiwan, 1062 subjects were recruited by 74 physicians from 35 hospitals, including general practitioners (3%), neurologists (42%), cardiologists (36%), internists (12%), endocrinologists (5%), general surgeons (1%), and angiologists (3%). The baseline demographic data of the Taiwanese population and the global subjects are listed in Table 1.

Table 1. Baseline demographics of Taiwan and global populations in the REACH Registry

	Population (%)**						
	Symptomatic (n = 971)	CAD (n = 541)	CVD (n = 496)	PAD (n = 29)	≥ 3 risk factors (n = 91)	Taiwan total (n = 1062) [†]	Global total (N = 67,888)
Age (yr), mean (SD)	66.01 (9.67)	65.68 (9.66)	66.50 (9.58)	69.57 (8.77)	69.16 (8.60)	66.27 (9.62)	68.5 (10.1)
Men	69.72	75.79	63.51	65.52	56.04	68.55	63.7
Diabetes [‡]	40.37	39.93	40.73	51.72	82.42	43.97 [‡]	44.3
Hypertension [§]	74.56	71.53	78.43	75.86	83.52 [‡]	75.33	81.8
Hypercholesterolemia	45.46	54.81	35.35	58.62	72.53	47.79	72.4
Abdominal obesity	22.26	20.78	24.02	13.79	27.59 [‡]	22.72	46.6
Waist circumference (cm), mean (SD)							
Men	91.80 (11.22)	92.25 (12.52)	91.34 (8.79)	90.45 (7.79)	92.44 (8.29) [‡]	91.85 (11.03)	99.70 (15.04)
Women	90.00 (16.96)	89.88 (13.19)	90.23 (18.71)	81.38 (11.90)	89.81 (9.61) [‡]	89.98 (16.24)	94.71 (17.37)
BMI							
<25	46.38	41.93	50.00	48.28	41.76 [‡]	45.98	30.0
25 – <30 (overweight)	42.65	45.27	41.26	41.38	43.96 [‡]	42.76 [‡]	39.8
Obesity							
Class I (BMI, 30 – <35)	9.32	10.76	7.32	10.34	10.99 [‡]	9.46	19.9
Class II (BMI, ≥35)	1.66	2.04	1.42	0	3.30 [‡]	1.80	10.3
Smoker							
Former	27.41	30.36	24.75	24.14	9.09	25.86	41.6
Current	17.57	18.41	16.63	10.34	21.59	17.91	15.3
Never	55.02	51.23	58.62	65.52	69.32	56.23	43.1

*p < 0.05 for comparisons between global and Taiwan populations; **p < 0.05 for comparisons between Taiwan symptomatic and risk factors only; [†]some patients with CAD, CVD or PAD are listed in 2 or 3 categories; [‡]patients with type 1 or 2 diabetes currently treated with hypoglycemic agents or history of diabetes; [§]patients currently treated with medication; ^{||}men: waist circumference ≥ 102 cm, women: waist circumference ≥ 88 cm; [†]p ≥ 0.05 (not significant). BMI = body mass index (calculated as weight in kilograms divided by the square of height in meters); CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; REACH = Reduction of Atherothrombosis for Continued Health.

The mean (SD) age of the Taiwanese subjects was 66.3 (9.62) years, and 68.6% of the total population were male. In comparison with global data in the REACH Registry, the Taiwanese population was younger (66.3 years *vs.* 68.5 years) and predominantly male (68.6% *vs.* 63.7%), had a lower prevalence of hypertension (75.3% *vs.* 81.8%), obesity (22.7% *vs.* 46.6% by waist circumference), and hypercholesterolemia (47.8% *vs.* 72.4%), had a lower prevalence of former smokers (25.9% *vs.* 41.6%), and a higher prevalence of non-smokers (56.2% *vs.* 43.1%), all reaching statistical significance ($p < 0.05$).

There were 91 (8.57%) asymptomatic patients with risk factors only (RFO). In comparison with the symptomatic group in Taiwan, the RFO group was older in age (69.2 years *vs.* 66.0 years), predominantly female (44.0% *vs.* 30.3%), with a higher prevalence of diabetes (82.4% *vs.* 40.4%), hypertension (83.5% *vs.* 74.6%), and hypercholesterolemia (72.5% *vs.* 45.5%), but a lower prevalence of former smokers (9.1% *vs.* 27.4%) and a higher prevalence of non-smokers (69.3% *vs.* 55.0%), all reaching statistical significance ($p < 0.05$).

Only 29 (2.7%) of the 971 symptomatic patients were diagnosed as having PAD. This percentage was much less than that of the global

population (2.7% *vs.* 14.9%, $p < 0.05$). In comparison with patients without PAD, PAD patients were older (69.6 years *vs.* 65.9 years), had a higher prevalence of diabetes (51.7% *vs.* 40.0%) and hypercholesterolemia (58.6% *vs.* 45.1%), a lower prevalence of obesity (13.8% *vs.* 22.5%), a lower prevalence of former smokers (24.1% *vs.* 27.5%), and a higher prevalence of non-smokers (65.5% *vs.* 54.7%) (data not shown).

Table 2 shows that, of the 1062 subjects, 90 (8.5%) had polyvascular disease. The proportion of patients with polyvascular disease was relatively lower in Taiwan than in the global population (8.5% *vs.* 15.9% in the total population and 9.5% *vs.* 19.5% in the symptomatic subjects).

Documented high blood pressure (systolic ≥ 140 mmHg and/or diastolic ≥ 90 mmHg), fasting hyperglycemia (glucose ≥ 126 mg/dL [6.99 mmol/L]), hypercholesterolemia (≥ 200 mg/dL [5.18 mmol/L]), and hypertriglyceridemia (≥ 150 mg/dL) were recorded in a substantial number of patients at baseline (Table 3). Hypertension was present in 46.5% (range, 39.6–53.4%; and highest in the CVD patients), fasting hyperglycemia in 38.5% (range, 36.9–57.7%; and highest in the RFO subjects), hypercholesterolemia in 45.8% (range, 44.9–59.3%; and highest in the PAD patients),

Table 2. Prevalence of polyvascular disease in the global and Taiwan REACH Registry populations

	Population (%) [*]	
	Global total	Taiwan total (n)
Single arterial bed		
Overall	65.9	83.0 (881)
CAD alone	44.6	42.7 (454) [†]
CVD alone	16.6	39.4 (418)
PAD alone	4.7	0.9 (9)
Polyvascular disease		
Overall	15.9	8.5 (90)
CAD + CVD	8.4	6.6 (70)
CAD + PAD	4.7	1.1 (12)
CVD + PAD	1.2	0.3 (3)
CAD + CVD + PAD	1.6	0.5 (5)
Multiple risk factors	18.3	8.6 (91)

^{*}Unless otherwise indicated, $p < 0.05$ for all comparisons; [†] $p \geq 0.05$ (not significant). CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; REACH = REDuction of Atherothrombosis for Continued Health.

Table 3. Undertreatment among patients in the global and Taiwan REACH Registry populations

	Population (%) [*]					Taiwan total (n = 1062)	Global total (N = 67,888)
	Symptomatic (n = 971)	CAD (n = 541)	CVD (n = 496)	PAD (n = 29)	≥ 3 risk factors (n = 91)		
Measured hypertension [‡]	46.32	39.63	53.36	48.28	48.89	46.54	49.97
Abnormal glycemia [§]	36.61	37.02	36.89	48.15	57.65	38.45	30.66
Abnormal cholesterol	45.51	44.90	46.58	59.26	48.31	45.77	39.28
Abnormal triglycerides [†]	42.28	41.14	45.39	62.96	48.31	42.83 [†]	44.21

^{*}Unless otherwise indicated, $p < 0.05$ for all comparisons between global and Taiwan populations; [†] $p \geq 0.05$ (not significant); [‡]measured hypertension $\geq 140/90$ mmHg; [§]abnormal glycemia ≥ 126 mg/dL; ^{||}abnormal cholesterol ≥ 200 mg/dL; [†]abnormal triglycerides ≥ 150 mg/dL. CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; REACH = REduction of Atherothrombosis for Continued Health.

and hypertriglyceridemia in 42.8% (range, 41.1–63.0%; and highest in the PAD patients) of the subjects.

Antihypertensive agents, hypoglycemic agents, lipid-lowering agents, and antiplatelet/anticoagulant medications were frequently used in these patients (Table 4). In the Taiwan REACH Registry, 95.2% of hypertensive patients received at least one antihypertensive agent—highest in CAD patients (97.8%) and lowest in PAD patients (91.7%)—which was lower than the 95.8% treatment rate in the global population. However, the Taiwanese population received antiplatelet agents more frequently than the global population (84.7% vs. 78.6%)—highest in the CAD patients (90.8%) and lowest in the PAD patients (69.0%). Diabetes medication and lipid-lowering agents were used less frequently in the Taiwanese population, attributed to the low prevalence of diabetes and hyperlipidemia.

Discussion

The REACH Registry is a global study which included subjects of different ethnicities and different populations at high risk for atherothrombotic diseases. These patients are expected to have a high probability of suffering disease recurrence or new atherothrombotic events in the future. The final results may demonstrate the long-term risks of atherothrombosis in the high-risk populations and will define the profile of subjects at risk for atherothrombosis and the predictors for

atherothrombotic events. By recruiting outpatients, subjects were able to visit medical clinics and tended to be stable, with mild morbidities, and good compliance with medications. These characteristics might lead to an underestimation of the endpoint events and undertreatment of the patients. However, baseline data from the Taiwan REACH Registry showed that there was a high proportion of treated patients not achieving therapeutic target levels for hypertension, diabetes and hyperlipidemia. The same observation applied to the global REACH Registry.⁶

The CAD and CVD mortality rates in Taiwan have decreased since 1994 (Figure).⁷ However, CVD and CAD were still the second and third leading causes of death in Taiwan in 2005, respectively.⁷ The annual mortality rate for CVD was 57.8 per 10⁵ (9.5% of all-cause mortality) and 57.1 per 10⁵ (9.3% of all-cause mortality) for CAD. Up to 18.8% of the unadjusted mortalities were from CVD and CAD,⁷ which is lower than the corresponding worldwide data of 24% in 2000.^{3,4} More aggressive therapeutic strategies to reach the treatment targets for risk factor control are required.

The recognition of most atherothrombotic risk factors was from studies conducted in North America⁵ or Europe.⁸ However, considerable data suggested that these risk factors varied in different areas and populations.⁹ For example, hypercholesterolemia is not a CAD risk factor in Indians¹⁰ as it is in people of European descent.⁹ The REACH Registry also provided a chance to evaluate the importance of variable risk factors in different subgroups. The Taiwan REACH Registry population

Table 4. Medication use among patients in the Taiwan and global REACH Registry populations

	Symptomatic (n = 971)	CAD (n = 541)	CVD (n = 496)	Population (%) [*]		
				PAD (n = 29)	≥ 3 risk factors (n = 91)	Taiwan total (n = 1062)
Global total (N = 67,888)						
Patients with diagnosed hypertension or elevated blood pressure at initial examination, n	787	416	424	24	79	866
At least 1 antihypertensive						
β-blockers	94.92 [†]	97.84	92.45	91.67	97.47	95.15
ACE inhibitors	43.26	55.77	32.62	37.50	34.62	42.48
Diuretics	20.74	23.08	17.26	12.50	23.68	21.00
Calcium channel blockers	21.91	24.34	21.51	33.33	28.21	22.48
Angiotensin II receptor blockers	52.16	52.16	54.14	41.67	55.13	52.43
Other antihypertensives	41.09	41.69	41.27	54.17	48.72	41.78
	8.92 [†]	10.14	8.49	16.67	8.86	8.91
Antiplatelet therapy						
At least 1 antiplatelet agent	87.74	90.76	85.28	68.97	51.65	84.65
Acetylsalicylic acid	60.25	63.96	55.04	37.93	32.97	57.91
Other antiplatelet agents	41.34	39.93	45.25	44.83	22.22	39.72
Patients with history of diabetes or elevated blood glucose at initial examination, n	456	261	231	17	76	532
At least 1 diabetes medication						
Sulfonylureas	78.46	74.33	81.74	88.24	96.05	80.98
Biguanides	62.36	58.91	64.16	58.82	70.83	63.53
Insulin	43.88 [†]	35.38	49.78	52.94	66.22	47.04
Thiazolidinediones	6.25	6.56	6.67	25.00	6.76	6.32
Other diabetes medications	16.96 [†]	19.53	12.83	37.50	38.16	20.04
	10.05 [†]	9.84	11.16	25.00	14.08	10.61
Nitrates	32.60	54.85	11.04	37.93	4.60	30.25
NSAIDs	6.78	4.49	9.47	6.90	5.81	6.70
Lipid-lowering therapy						
At least 1 agent	49.54	59.70	39.11	62.07	68.13	51.13
Statin	43.25	51.02	34.88	51.72	64.84	45.10
Other lipid-lowering agents	7.42	10.17	4.84	10.34	6.59	7.34

^{*}Unless otherwise indicated, $p < 0.05$ for all comparisons; [†] $p \geq 0.05$ (not significant). CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; REACH = Reduction of Atherothrombosis for Continued Health; ACE = angiotensin-converting enzyme; NSAID = nonsteroidal anti-inflammatory drugs.

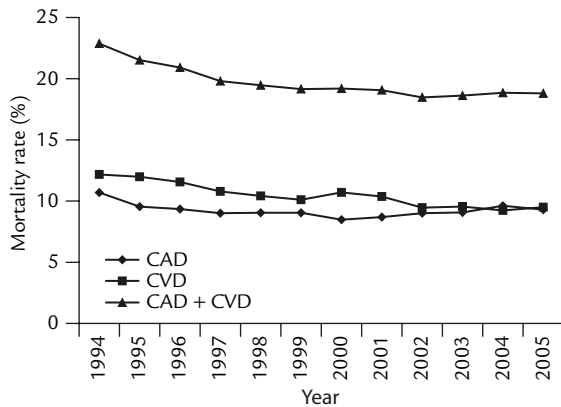


Figure. Mortality trends in patients with cardiovascular disease (CAD) and cerebrovascular disease (CVD) in Taiwan, 1994–2005. [Source: Reference 7.]

had a high prevalence of hypertension and diabetes, similar to that of the global REACH Registry population, but a significantly lower prevalence of obesity (either by waist circumference or by BMI criteria), hypercholesterolemia, and a higher proportion of non-smokers. These results partially explained the lower mortality rates for CAD and CVD in Taiwan. In the Taiwan REACH Registry population, there was also a significantly higher prevalence of non-smokers in the RFO group than in the symptomatic group, a significantly higher prevalence of hypertension, diabetes, and hypercholesterolemia, and a slightly higher prevalence of obesity in the RFO group. Smoking was probably not only an independent risk factor for atherothrombosis, but also has a synergistic effect in causing atherothrombotic events.

Smoking is a general risk factor for atherothrombotic disease. Smoking accounted for a population attributable risk (PAR) of 35.7% with an odds ratio (OR) of 2.87 for current and former versus non-smokers in the CAD population.¹¹ This effect was lower than increased apolipoprotein (Apo) B/ApoA1 ratio (PAR, 49.2; OR, 3.25), and higher than hypertension (PAR, 17.9; OR, 1.91), diabetes (PAR, 9.9; OR, 2.37), and abdominal obesity (PAR, 20.1; OR, 1.12) as seen in the global REACH Registry baseline data.¹² Active smokers have up to an 80% increased risk of CAD and passive smokers have at least a 30% increased risk of CAD.¹² Smoking was also a risk factor for CVD

with an event attributable risk of 30% for current smokers in Japan.¹³ The total excess relative risk (RR) of stroke was 1.6 (95% confidence interval [CI], 1.1–2.4), and up to 2.3 (95% CI, 1.2–4.4) in hypertensive patients.¹³ Smoking could contribute to 50% symptomatic PAD with a dose-dependent increased prevalence of 2.3-fold in current smokers and 2.6-fold in former smokers.¹⁴ Smokers of all ages have a two-to-three times higher death rate than non-smokers.⁴ CAD was the leading cause of smoking-related premature death.¹⁵ It was estimated that 1.69 million of the deaths were caused by CAD, accounting for 11% of total global CAD deaths.¹⁵ Smoking cessation will decrease the risk of CAD with a hazard ratio (HR) of 0.71 (95% CI, 0.64–0.78) and ischemic stroke with a HR of 0.84 (95% CI, 0.76–0.92).¹⁶ In the Taiwan REACH population, the prevalence of former and current smokers was 44.8%, which was higher than the 39.88% of Taiwan smoking prevalence in men in 2005¹⁷ and 20–30% smoking prevalence in Western countries.¹⁸ In order to decrease atherothrombotic morbidity and mortality, smoking abstinence and cessation should be strongly encouraged.

The prevalence of obesity is increasing and has become a global public health problem. Overweight and obesity increase CAD risk by 1.40- to 1.65-fold in men and 1.32- to 1.83-fold in women, respectively.¹⁹ Obesity also increases CVD risk by 1.86-fold in men and 1.21-fold in women.²⁰ Each one-unit increase in BMI increases the multiple adjusted risk of ischemic stroke and hemorrhagic stroke by 4% and 6%, respectively.²¹ Epidemiologic data suggest that the same BMI in different ethnicities and races represent different risks. For example, the Asian American population with BMI < 25 kg/m² had a high percentage of metabolic risk factors and abdominal obesity.²² A study found that the relationship between percent body fat and BMI differs between different ethnic groups. For the same level of body fat, age and gender, the BMIs of Chinese, Ethiopians, Indonesians and Thais are 1.9, 4.6, 3.2 and 2.9 kg/m² lower compared to Caucasians.²³ In the REACH Registry, overweight, obesity, and abdominal obesity were

based on the WHO definition.^{24,25} Since this definition makes no allowance for different ethnic groups, baseline data from the Taiwan REACH Registry reported a low prevalence of obesity. Therefore, in order to accurately assess the obesity risk in the Taiwan REACH Registry, it is necessary to establish an obesity index appropriate for the Taiwanese population based on regional considerations.

Only 29 (2.7%) PAD subjects were identified either with PAD alone or with polyvascular diseases in the Taiwan REACH Registry, attributed to a very low ABI examination rate. This prevalence was lower than the 14.9% in the global REACH Registry and that of the general population which was estimated at about 3.9% in males and 3.3% in females²⁶ and was highly age-dependent, with a range from 2.5% in people <60 years of age, 8.3% in the 60–69 year age group, and up to 18.8% in those ≥ 70 years of age.²⁷ The prevalence increased to 29% in primary care clinics and only 49% of them were aware of PAD by physician.²⁸ Comorbidities of CAD or CVD are common in PAD patients. Based on the PARTNERS program, about 44% of PAD patients from primary care clinics had PAD alone and 56% of PDA patients had PAD combined with CAD.²⁸ The prevalence of CVD in PAD patients varied between 0.5% and 15% by history and would be up to 90% by angiography.²⁹ The long-term risk for large vessel PAD patients is very high, with a RR of 3.1 in all-cause mortality, 5.9 in cardiovascular deaths, and 6.6 in CAD deaths; the mortality rate would increase 15-fold if PAD was both severe and symptomatic in 10 years of follow-up.³⁰ However, PAD patients frequently receive inadequate risk factor control and antiplatelet treatment,^{28,30} and would have a poorer hospital outcome following an acute coronary event.³¹ Low awareness and undertreatment of PAD is likely to be a universal problem. Therefore, the identification and treatment of PAD as well as CAD and CVD could reduce atherothrombotic morbidity and mortality.

In conclusion, the baseline data from the Taiwan REACH Registry show that outpatients with documented atherothrombotic disease or

multiple risk factors were largely undertreated for risk factor control, and PAD patients were underdiagnosed. Therefore, strategies for risk factor control, for example, smoking and obesity, should be introduced in an effort to reduce atherothrombotic risk in the Taiwanese population.

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References

1. Viles-Gonzalez JF, Fuster V, Badimon JJ. Atherosclerosis: a widespread disease with unpredictable and life-threatening consequences. *Eur Heart J* 2004;25:1197–207.

2. Libby P. The interface of atherosclerosis and thrombosis: basic mechanisms. *Vasc Med* 1998;3:225–9.
3. Ohman EM, Bhatt DL, Steg PG, et al. The REduction of Atherothrombosis for Continued Health (REACH) Registry: an international, prospective, observational investigation in subjects at risk for atherothrombotic events—study design. *Am Heart J* 2006;151:786.e1–10.
4. World Health Organisation. *Reducing Risks, Promoting Healthy Life. The World Health Report. 2002*. Geneva: WHO.
5. Vasan RS, Massaro JM, Wilson PWF, et al. Antecedent blood pressure and risk of cardiovascular disease; the Framingham heart study. *Circulation* 2002;105:48–53.
6. Bhatt DL, Steg PG, Ohman EM, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA* 2006;295:180–9.
7. Department of Health, Executive Yuan, Taiwan, R.O.C. *Causes of Death Statistics, 1994–2005*. Available from www.doh.gov.tw/statistics/index.htm [Date accessed: August 18, 2006]
8. Yusuf S, Reddy S, Ôunpuu S, et al. Global burden of cardiovascular disease, part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 2001;104:2746–53.
9. Yusuf S, Reddy S, Ôunpuu S, et al. Global burden of cardiovascular diseases part II: variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. *Circulation*. 2001;104:2855–64.
10. Pais P, Pogue J, Gerstein H, et al. Risk factors for acute myocardial infarction in Indians: a case-control study. *Lancet* 1996;348:358–63.
11. Yusuf S, Hawken S, Ôunpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937–52.
12. Law MR, Morris JK, Wald NJ. Environmental tobacco smoke exposure and ischemic heart disease: an evaluation of the evidence. *BMJ* 1997;315:973–80.
13. Yamagishi K, Iso H, Kitamura A, et al. Smoking raises the risk of total and ischemic strokes in hypertensive men. *Hypertens Res* 2003;26:209–17.
14. Willigendael EM, Teijink JAW, Bartelink ML, et al. Influence of smoking on incidence and prevalence of peripheral arterial disease. *J Vasc Surg* 2004;40:1158–65.
15. Ezzati M, Lopez AD. Estimates of global mortality attributable to smoking in 2000. *Lancet* 2003;362:847–52.
16. Asia Pacific Cohort Studies Collaboration. Smoking, quitting, and the risk of cardiovascular disease among women and men in the Asia-Pacific region. *Int J Epidemiol* 2005;34:1036–45.
17. Bureau of Health Promotion, Department of Health, Taiwan, ROC. *Taiwan Tobacco Control Annual Report, 2006*. Taipei: Bureau of Health Promotion, Department of Health, Taiwan, ROC, June 8, 2006.
18. Woo KS, Yip TWC, Kwong SK, et al. Commentary: smoking and atherosclerotic diseases in Asia—the implication in global atherosclerosis prevention. *Int J Epidemiol* 2005;34:1045–6.
19. Mcgee DL, The diverse populations collaboration. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observation studies. *Ann Epidemiol* 2005;15:87–97.
20. Wilson PWF, D'Agostino RB, Sullivan L, et al. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Intern Med* 2002;162:1867–72.
21. Poirier P, Giles TD, Bray GA, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss. *Arterioscler Thromb Vasc Biol* 2006;26:968–76.
22. Ko GTC, Chan JCN, Cockram CS, et al. Prediction of hypertension, diabetes, dyslipidaemia or albuminuria using simple anthropometric indexes in Hong Kong Chinese. *Int J Obes Relat Metab Disord* 1999;23:1136–42.
23. Deurenberg P, Yap M, van Staveren WA. Body mass index and percent body fat: a meta-analysis among different ethnic groups. *Int J Obes Relat Metab Disord* 1998;22:1164–71.
24. World Health Organisation. *Obesity: Preventing and Managing the Global Epidemic. Report on a WHO Consultation on Obesity, Geneva, 3–5 June 1997*. Geneva: WHO/NUT/NCD/98.1, 1998.
25. World Health Organisation. *Physical Status: The Use and Interpretation of Anthropometry*. Geneva: WHO, 1995, Technical Report Series 854.
26. Murabito JM, Evans JC, Nieto K, et al. Prevalence and clinical correlates of peripheral arterial disease in the Framingham offspring study. *Am Heart J* 2002;143:961–5.
27. Criqui MH, Fronek A, Barrett-Connor E, et al. The prevalence of peripheral arterial disease in a defined population. *Circulation* 1985;71:510–5.
28. Hirsch AT, Criqui MH, Diane TJ, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2001;286:1317–24.
29. Dormandy J, Mahir M, Ascady G, et al. Fate of the patient with chronic leg ischaemia. A review article. *J Cardiovasc Surg (Torino)* 1989;30:50–7.
30. Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med* 1992;326:381–6.
31. Froehlich JB, Mukherjee D, Avezum A, et al. Association of peripheral artery disease with treatment and outcomes in acute coronary syndromes. The global registry of acute coronary events (GRACE). *Am Heart J* 2006;151:1123–8.